

Intradermal Delivery of Methylene Blue using hMTS for Sentinel Lymph Node Mapping

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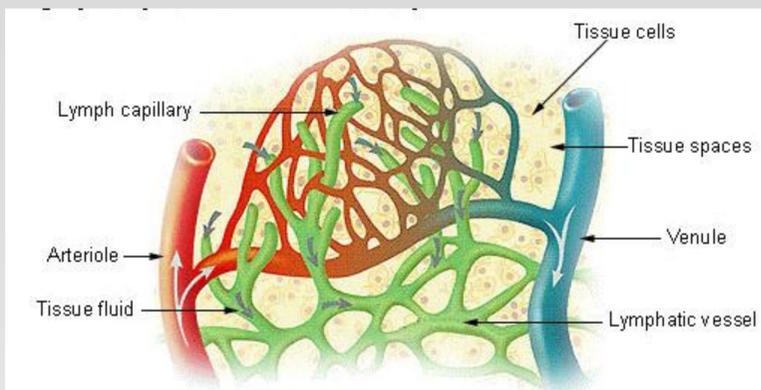
BACKGROUND & PURPOSE

Sentinel lymph node biopsy (SLNB) has emerged as a new standard for staging breast cancer. Methylene blue (MB) is routinely used as a dye for mapping the sentinel lymph node associated with a tumor. Among available delivery routes, intradermal delivery is of interest due to the lymphatic capillaries that perfuse the intradermal compartment. However, intradermal delivery of a 1% MB solution using conventional intradermal injection techniques may cause significant discomfort and skin necrosis. Thus, there is motivation to revisit the MB dose and method of intradermal administration to identify conditions for effective SLN staining.

METHODS

3M has developed a hollow Microstructured Transdermal System (hMTS), a hollow microneedle delivery device, that can deliver up to 2 mL of formulation into the intradermal space. A variety of solutions with various concentrations of MB were delivered intradermally to domestic swine and Sprague Daley rats to assess lymphatic staining and skin tolerability. The delivery sites were observed over a course of 2 weeks. To determine the extent of MB staining of lymph nodes, swine and rats were dissected to trace the MB distributed inside the body. SLN was identified and isolated based on the blue color stain associated with MB ID delivery.

Lymph Capillaries in the Tissue Spaces



Source: U.S. National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Program

hMTS Delivery Systems



A) Hollow microneedle array (hMTS); B) hMTS injector and cartridges filled with methylene blue solution ; C) Quick Evaluation Device for controllable delivery of liquid formulation.

Skin Recovery Followed by Intradermal Delivery of Methylene Blue in Swine

DAY 0



DAY 7

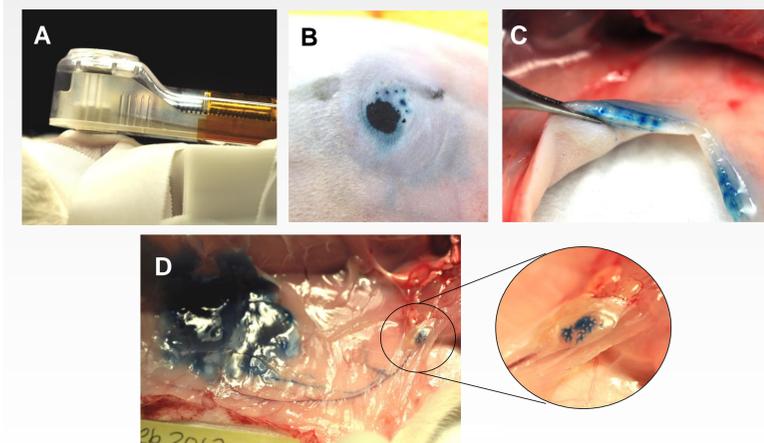


DAY 12



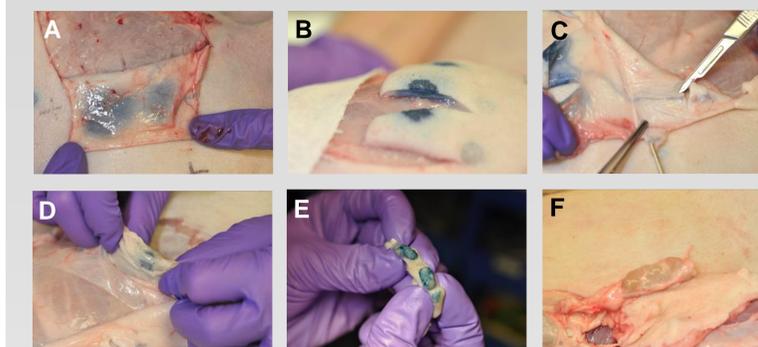
Methylene blue (0.05%) was injected intradermally into swine using hollow microneedles. After 12 days, the skin recovered without necrosis.

Sentinel Lymph Node Mapping in Rats



A) hMTS injector following 1 ml ID delivery in a rat; B) delivery site (rat); C) cross sectional view of delivery site; D) stained lymphatic capillary and sentinel lymph node.

Sentinel Lymph Node Mapping in Swine



A) Swine skin was cut and flipped over to verify ID delivery; B) The delivery site was cut in half to see the cross section of the dermis; C) The lymphatic capillary draining the MB injection site was identified based on the blue stain; D) The sentinel lymph node was located by tracing the blue stain; E) The stained sentinel lymph node was cut open to verify the staining; F) A nearby lymph node, not draining the delivery site, was isolated and showed no signs of blue staining.

CONCLUSION

Intradermal delivery of low concentration methylene blue solution (<1%) using a hollow microneedle device effectively mapped the sentinel lymph node. Good skin tolerability was achieved.